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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,627	11/23/2001	George Jackowski	2132.106	4724

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EXAMINER	
CHEU, CHANGHWA J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,627	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 39-46* is/are pending in the application.

4a) Of the above claim(s) *39-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 1/10/2005 has been received and entered. Applicant elects group I, claims 1 with traverse has been entered into record. The status of the current claims are as follows:

1. Claim 1 is amended.
2. Claims 2-38 are cancelled.
3. Claims 39-46 are added.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
   - I. Claim 1, drawn to a biopolymer consisting of the SEQ ID No. 2, classified in class 530, subclass 350.
   - II. Claims 39-43, drawn to a method comparing peptide profile of patient samples to SEQ ID No. 2, classified in class 436, subclass 518.
   - III. Claims 44-46, drawn to a kit comprising the peptide consisting of SEQ ID No. 1 and antibodies to the bind the peptide, classified in class 422, subclass 61.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the peptide SEQ ID No.2 of invention I can be used in other materially different processes, such as identification or isolation other than using MS protein profiling.

3. Inventions I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions invention I directs to a peptide whereas invention II requires an antibody.

Furthermore, both peptide and antibody are structurally and functionally distinct and requires separate search.

4. Inventions II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the kit of invention III can be used to practice materially different method such as isolation or purification of SEQ ID No. 2 peptide other than the MS protein profiling in invention II.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, and the search required for one group is not required for the other, restriction for examination purposes as indicated is proper.

6. Applicant's election of invention I (claim 1) with traversal on the ground that amino acid sequences numbered one through four (SEQ ID No. 1-4) are related as a Markush-type grouping because they share a common utility, therefore the sequences should not be restricted. This traversal was carefully considered but not persuasive. Although the sequences of the SEQ ID No. 1-4 do have a common utility, nevertheless they *do not share a substantial structural feature* disclosed as being essential to that utility (emphasis added). MPEP 803.02 requires that Markush groups share common utility *and* a substantial structural feature disclosed as being essential to that utility.
The requirement is still deemed proper and is therefore made **FINAL.**

6. Claims 39-46 are withdrawn from further consideration pursuant to 37 CFR 1 .142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10 December 2004.

7. Currently claim 1 is under consideration.

Oath and Declaration

8. A new oath or declaration is required because the date for Dr. John Marshall (inventor 2) is omitted. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmation have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP jj 602.01 and 602.02.

Abstract

9. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

10. The instant application includes legal phraseology "said". Appropriate correction is required.

Claim Rejections - 35 USC § 112

Enablement

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2)

the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

Claim 1 directs to biopolymer consisting of SEQ ID NO. 2 capable of diagnosing Insulin Resistance patient (IR). However, in view of the specification, the disclosed information is not sufficient to enable one ordinary skill in the art to use such information without undue experimentation.

Applicant presents 3 sets of data in support of the recited feature, namely the SEQ ID No. biopolymer can be used to detect IR patient. The first data is from Figure 1 which is a photograph of a gel for both normal people versus the IR patients. The second and third data is a mass/ion spectrophotometry analysis of the trypsin-digested peptide profile (See Figure 2 and 3). Nevertheless, the most crucial result, i.e. Figure 1, fails to show any correlation between the IR disease state and the SEQ ID No. 2.

Data from Figure 1 are not clear in several aspects. First, it is not clear how many samples are involved in the experiments. Assuming 16 samples are for each normal and IR patients (See the upper top of Figure 1). With this information, the bands appear on the gel still remains further characterization. Focusing on IR gel, it is not clear what "C2B", "C10", "C6", "C12", "C13B" or "C15" represent for. Are these "C2B", "C10", "C6", "C12", "C13B" or "C15" from one of the SEQ ID Nos? If this is the case, it would raise questions concerning "specificity", i.e. false positive. For instance, the Figure 1 gel for IR shows many bands, some of them do not appear in the normal patients. However, within this IR region (gel), some of the bands appear in some IR patients, but not other IR. Most importantly, there is no information concerning each band as to what SEQ ID Nos each band corresponding. In another word, applicant has not set forth any supporting evidence that suggests that SEQ ID No. 2 is a unique

molecular marker for IR. The results would not be useful to one ordinary skill in the art to identify IR patients.

Furthermore, Tascilar et al. (Annals of Oncology 10,Suppl. 4:S107-S1-10, 1999) reports on diagnostic methods in the realm of disease states. It is well- known that molecular-based assays are valid tools use in predicting and detecting diseases, however as assessed in the Tascilar review ". . .these tests should be interpreted with *caution*. . . " and the genetic changes found in sources other than the pancreas itself (blood, stool) should be evaluated *prudently*" (page S2, right colume)(emphasis added).

Tockman et al. also teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application (Cancer Research 52:2711s-2718s, 1992). Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles for biomarkers taught are clearly applicable to other oncogenic disorders. Tockman et al. teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, (See abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, column 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cpology-confrmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link those marker results with subsequent histological confirmation of disease. "This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]" (See page 2714s, column 1, Biomarker Validation against Acknowledged Disease End Points section). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged

disease end points and the marker predictive value must be confirmed in prospective population trials (See page 2716s, column 2, Summary section). Tockman et al. reiterates that the predictability of the art in the regards to cancer prognosis and the estimation of life experience within a population with a disease or disorder are *highly speculative* and *unpredictable.* Supra.

In view of the teachings of In re Wands, 8 USPQZd 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966). While every aspect of a generic claim does not have to be carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Genetech Inc. v. Novo Nordisk A/S ICAFCI 42 USPQZd 1001. That requirement has not been met in this specification with respect to the biopolymer consisting of SEQ ID NO:2 diagnostic for Insulin Resistance. Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims and to practice the invention as claimed.

Conclusion

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

February 4, 2005

LONG V. LE
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03/04/05